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# Dopaminergic cells repolarization induced by calcium and $Na^+/K^+$ ATPase pumps

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The firing pattern in dopaminergic (DA) neurons influences the extracellular concentration of dopamine in projection areas. A burst produces a greater phasic increase in dopamine concentration than a tonic one [1]. Burst firing of midbrain dopamine neurons is associated with behavioral motivation and reward mechanisms. At the same time, dopamine pathway, which is one of the oldest responsible for biological survival and present even in worms and flies, is profoundly altered by cocaine. In particular, limbic system, which controls emotional responses and links them with memories, has it most cocaine-sensitive site located in nucleus accumbens. Parkinson's disease (PD) is one of the most common diseases among the aging and affects approximately 1% of the population worldwide [2]. There is no known cure for PD, and with an ageing population as the average life span increases due to a general improvement in health care, understanding the cause and progression of the neurodegenerative process is as challenging as it is necessary. In PD, neurons of the substantia nigra pars compacta progressively degenerate and when about 50% of them are lost the amount of dopamine available for neurotransmission in the corpus striatum is lowered by 80% the external signs of the disease are apparent. PD is not simply due to dopamine deficit, but is rather a multisystem disorder. For example, norepinephrine may play a key role in compensating for DA neurons lose in the early stages of the disease [3]. Therefore, understanding the mechanism of tonic and burst firing in DA neurons may lead to a better understanding and possible solutions for a series of neurodegenerative diseases.

We previously refined [4] a single-compartment Hodgkin-Huxley (HH) computational model of DA neurons closely following previous work done by Amini [5]. The model included only three essential currents: 1) a low voltage-activated calcium current $I_{CaL}$, tentatively identified as L-type $Ca^{2+}$, with a sigmoidal voltage-dependent activation function with $V_{1/2}$=-45 mV and a slope of $V_{slope}$=7mV and no inactivation, 2) an apamin sensitive small-conductance calcium-activated potassium current $I_{SK}$ with a Michaelis-Menten kinetics and a half-activation concentration of 190 nM, and 3) a slowly activating potassium current $I_{K(ERG)}$ tentatively identified as an as ether-a-go-go (ERG) current. The above model rely on $I_{CaL}$ to provide the depolarization whereas the repolarization of the cell is provided by a) the apamin-sensitive potassium current $I_{SK}$ during the tonic firing, or b) the $I_{K(ERG)}$ during the burst firing. We subsequently investigated the effects on the firing patterns of 1) the electrogeneicity of $Ca^{2+}$ pump, and 2) the homeostatic effect of Na/K ATPase pump [6,7]. We found that a totally nonelectrogenic $Ca^{2+}$ pump helps repolarizing the DA cell. However, a bifurcation diagram using the electrogeneicity of $Ca^{2+}$ pump as bifurcation parameter reveals that it can also contribute to cell depolarization. The $Na^+/K^+$ ATPase pump is central to neuronal survival, in maintaining resting membrane potential and influencing the pattern of firing activity of nigral neurons. We found a significant contribution of $Na^+/K^+$ ATPase pump to cell repolarization, which together with $Ca^{2+}$ pump contribution, could significantly diminish the role of $I_{K(ERG)}$ in cell repolarization.

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